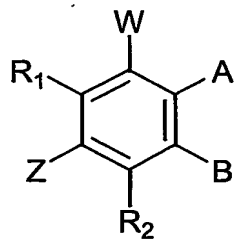
Claims

1. A method of increasing the sensitivity of cancer cells or a tumour to a chemotherapeutic agent by contacting said cells or tumour with an isoflavonoid compound of formula (I):

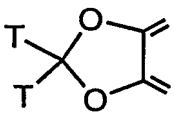


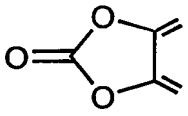
(I)

in which

R_1, R_2 and Z are independently hydrogen, hydroxy, OR_9, $OC(O)R_{10}$, $OS(O)R_{10}$, CHO, $C(O)R_{10}$, COOH, CO_2R_{10}, $CONR_3R_4$, alkyl, haloalkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, alkylaryl, alkoxyaryl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or

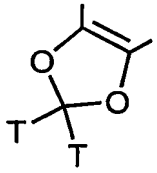
R_2 is as previously defined, and R_1 and Z taken together with the carbon atoms to which they are attached form a five-membered ring selected from

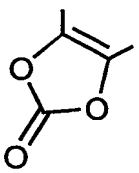




, or

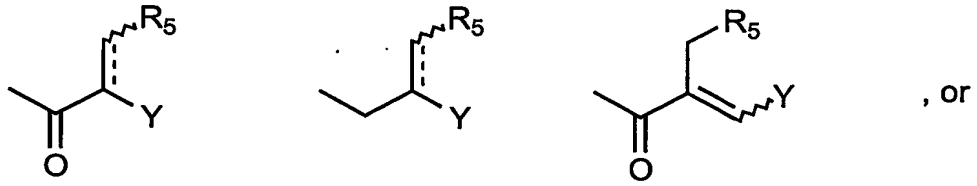
R_1 is as previously defined, and R_2 and Z taken together with the carbon atoms to which they are attached form a five-membered ring selected from





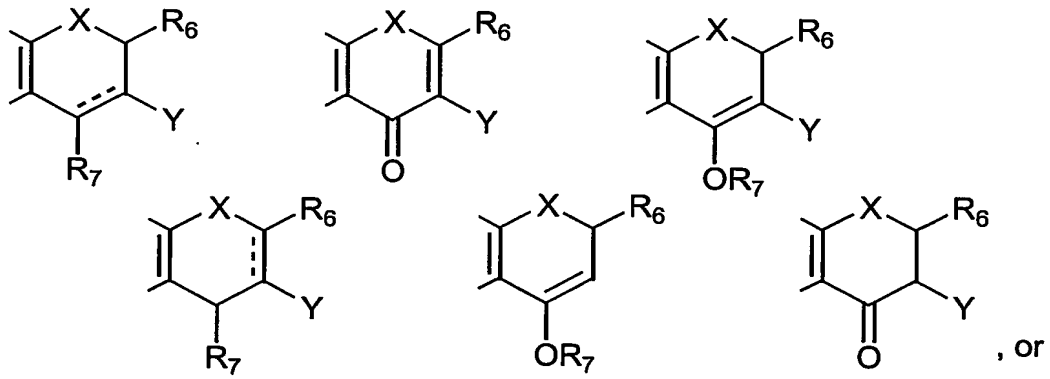
and

W is R_1, A is hydrogen, hydroxy, NR_3R_4 or thio, and B is selected from



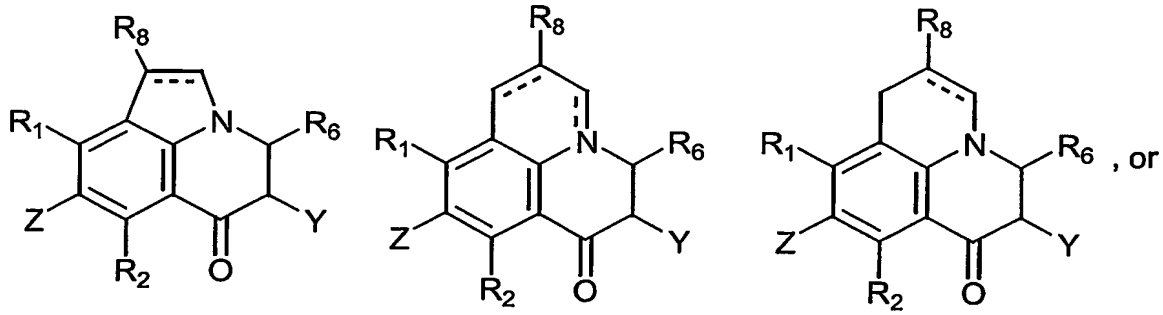
, or

W is R_1, and A and B taken together with the carbon atoms to which they are attached form a six-membered ring selected from



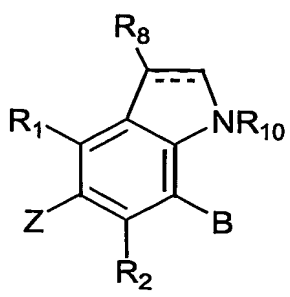
, or

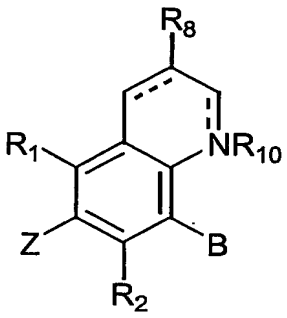
W, A and B taken together with the groups to which they are associated are selected from

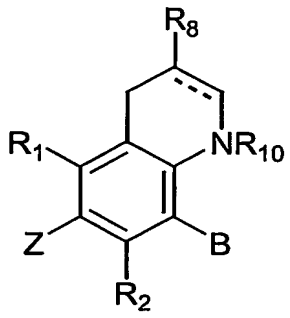


, or

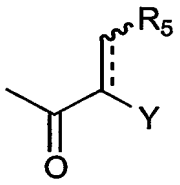
W and A taken together with the groups to which they are associated are selected from

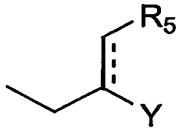


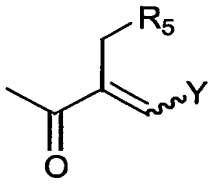




and B is selected from







wherein

R_3 is hydrogen, alkyl, arylalkyl, alkenyl, aryl, an amino acid, $C(O)R_{11}$ where R_{11} is hydrogen, alkyl, aryl, arylalkyl or an amino acid, or CO_2R_{12} where R_{12} is hydrogen, alkyl, haloalkyl, aryl or arylalkyl,

R_4 is hydrogen, alkyl or aryl, or

R_3 and R_4 taken together with the nitrogen to which they are attached comprise pyrrolidinyl or piperidinyl,

R_5 is hydrogen, $C(O)R_{11}$ where R_{11} is as previously defined, or CO_2R_{12} where R_{12} is as previously defined,

R_6 is hydrogen, hydroxy, alkyl, aryl, amino, thio, NR_3R_4, COR_{11} where R_{11} is as previously defined, CO_2R_{12} where R_{12} is as previously defined or $CONR_3R_4$,

R_7 is hydrogen, $C(O)R_{11}$ where R_{11} is as previously defined, alkyl, haloalkyl, alkenyl, aryl, arylalkyl or $Si(R_{13})_3$ where each R_{13} is independently hydrogen, alkyl or aryl,

R_8 is hydrogen, hydroxy, alkoxy or alkyl,

R_9 is alkyl, haloalkyl, aryl, arylalkyl, $C(O)R_{11}$ where R_{11} is as previously defined, or $Si(R_{13})_3$ where R_{13} is as previously defined,

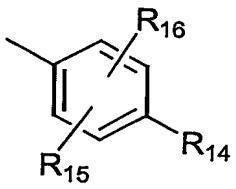
R_{10} is hydrogen, alkyl, haloalkyl, amino, aryl, arylalkyl, an amino acid, alkylamino or dialkylamino,

the drawing "---" represents either a single bond or a double bond,

T is independently hydrogen, alkyl or aryl,

X is O, NR_4 or S, and

Y is



wherein

R_{14}, R_{15} and R_{16} are independently hydrogen, hydroxy, OR_9, $OC(O)R_{10}$, $OS(O)R_{10}$, CHO, $C(O)R_{10}$, COOH, CO_2R_{10}, $CONR_3R_4$, alkyl, haloalkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or any two of R_{14}, R_{15} and R_{16} are fused together to form a cyclic alkyl, aromatic or heteroaromatic structure,

and pharmaceutically acceptable salts thereof.

2. A method of claim 1, wherein the sensitivity of the cancer cells or tumour to the chemotherapeutic agent is restored.

3. A method of claim 1, wherein the compound of formula (I) is administered to a subject in need of such treatment

4. A combination therapy for the treatment, prophylaxis, amelioration, defence against and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress comprising administering to a subject a therapeutically effective amount of a compound of formula (I) as defined in claim 1 and a chemotherapeutic agent.

5. A method for the treatment, prophylaxis, amelioration, defence against and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress which method includes the step of administering a compound of formula (I) and a chemotherapeutic agent.

6. A method of claim 5, wherein the cancer is selected from breast cancer, prostatic cancer, testicular cancer, ovarian cancer, uterine cancer and colorectal cancer.

7. A method claim 6, wherein the cancer is selected from ovarian cancer, prostatic cancer and pancreatic cancer.

8. A method of claim 5, wherein the administration of the compound of formula (I) precedes the administration of the chemotherapeutic agent.

9. A method of claim 5, wherein the administration of the compound of formula (I) and the chemotherapeutic agent is simultaneous.

10. A method claim 5, wherein the combination therapy follows observed resistance by cancer cells or tumour to a chemotherapeutic agent.

11. A method of claim 5, wherein the compound of formula (I) is an isoflav-3-ene of general formula (VIa).

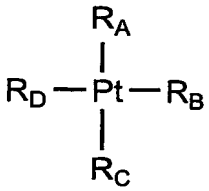
12. A method of claim 11, wherein the compound is dehydroequol.

13. A method of claim 5, wherein the chemotherapeutic agent is cisplatin, paclitaxel or carobplatin.

14. Use of a compound of formula (I) and a chemotherapeutic agent in the manufacture of a medicament for the treatment of cancer or a disease associated with antioxidant stress.

15. A pharmaceutical agent comprising a compound of formula (I) and an anticancer agent.

16. A platinum-isoflavonoid complex or analogue thereof of the general formula (II):



(II)

in which

R_A, R_B, R_C, and R_D are independently halo, hydroxy, XR_E, alkoxy, $OC(O)R_F$, $OS(O)R_F$, thio, alkylthio, amino, alkylamino or dialkylamino,

X is O, NR_F or S, and

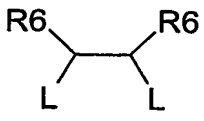
R_F is hydrogen, alkyl, arylalkyl, alkenyl, aryl or an amino acid,

wherein

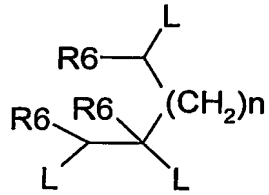
at least one of R_A, R_B, R_C, and R_D, and preferably only R_A, is XR_E where R_E is an isoflavonoid compound represented by general formula (I) set out above or is derived from or is a radical or ion of the isoflavonoid compound (I) and ligates to the platinum through any one or more of the heteroatoms X or a radical of the heteroatoms defined as part of R_E or alternatively by a double bond on the isoflavonoid compound (I)

and

when R_A is XR_E, R_B, R_C and/or R_D together may form part of a bidentate or tridentate ligand of general formulae (B) and (T) respectively



(B)



(T)

wherein L represents a ligating atom chosen from N, O and S,
n is from 0 to 8, and
each R_6 is independently as defined above or may together form part of a cyclic alkyl, aromatic or heteroaromatic structure,

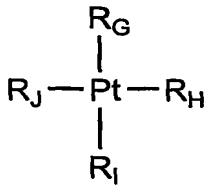
which platinum-isoflavonoid complexes include pharmaceutically acceptable salts thereof.

17. A method for the treatment, prophylaxis, amelioration, defence against, and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress which method comprises administering to a subject a therapeutically effective amount of one or more platinum-iosoflavanoid complexes of the formula (II) as defined above.

18. Use of platinum isoflavonoid complexes of the formula (II) for the manufacture of a medicament for the treatment, amelioration, defence against, prophylaxis and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress.

19. A pharmaceutical composition comprising one or more platinum-isoflavonoid complexes of the formula (II) in association with one or more pharmaceutical carriers and/or excipients.

20. A composition comprising a platinum complex of the general formula (IIa),



(IIa)

in which

R_G, R_H, R_I, and R_J are independently halo, hydroxy, alkoxy, $OC(O)R_K$, $OS(O)R_K$, thio, alkylthio, amino, alkylamino or dialkylamino,

X is O, NR_K or S, and

R_K is hydrogen, alkyl, arylalkyl, alkenyl, aryl or an amino acid,

in association with an isoflavonoid compound of general formula (I) as defined in claim 1 and pharmaceutically acceptable salts thereof.

21. A method for the treatment, prophylaxis, amelioration, defence against, and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress which comprises administering to a subject a therapeutically effective amount of a composition of claim 20.

22. Use of a platinum complex of the formula (IIa) and an isoflavonoid compound of the formula (I) in the manufacture of a medicament for the treatment, amelioration, defence against, prophylaxis and/or prevention of cell proliferation, cancer or a disease associated with oxidant stress.